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A MANNICH-TYPE REACTION OF CYCLOPROPANONE*

by

W.J.M. van Tilborg**, G. Dooyewaard, H. Steinberg and Th.J. de Boer***

Laboratory of Organic Chemistry, University of Amsterdam,

Nieuwe Achtergracht 129, Amsterdam, The Netherlands

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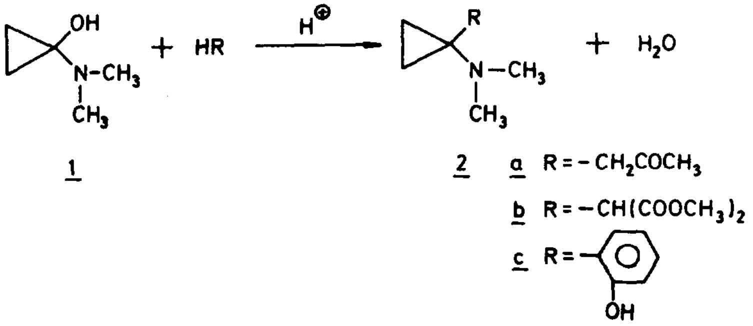
We have previously reported[1] on the similarity in chemical behaviour of cyclopropanone and formaldehyde. In order to extend this analogy, we have examined the possibility of using cyclopropanone in Mannich-type reactions.

A recent paper of Wasserman et al.[2] on related "cyclopropanone precursors in the bicyclo[4.1.0] series" prompts us to report our results.

The well known Mannich reaction[3,4,5] between formaldehyde, secondary amines and substrates containing "activated hydrogen" is supposed to proceed via a 1-amino-alcohol. The adduct of dimethylamine to cyclopropanone 1, which can be isolated in good yield[6], is a convenient "starting material".



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[*] Part of the thesis of W.J.M. van Tilborg, University of Amsterdam, 1971.

[**] Present address: Koninklijke/Shell Laboratorium, Badhuisweg 3, Amsterdam.

[***] From whom reprints may be obtained.

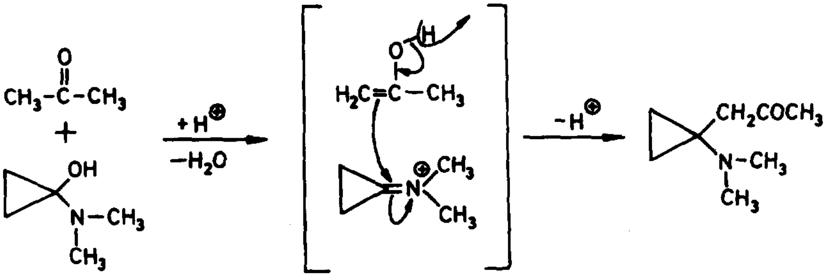
Thus, if 1-dimethylaminocyclopropanol 1, acetone and acetic acid, in a molar ratio of 2:4:3, are heated for 20 hrs to 65°, the corresponding Mannich base 2a is isolated in 33% yield by pouring the reaction mixture into water (pH > 11) and extracting repeatedly with ether. 1-Dimethylaminocyclopropylacetone 2a: Analysis calc. for $C_8H_{15}ON$: C 68.04; H 10.71; O 11.33; N 9.92, Found C 67.89; H 10.68; O 11.47; N 9.99

IR (liq. film): 3105, 3020 cm^{-1}, cyclopropyl C-H; 3000, 2960, 2870, 2830, 2780 cm^{-1}, $N(CH_3)_2$; 1700 cm^{-1}, C=O; 1020 cm^{-1}, cyclopropyl

NMR ($CDCl_3$): δ = 0.65 ppm, AA'BB' pattern (4H); δ = 2.20 ppm, s (3H); δ = 2.29 ppm, s (6H) and δ = 2.55 ppm, s (2H)

MS: $M^{\oplus}$ at m/e 141, 14.5% of the base peaks at m/e 98 and m/e 44.

When the molar ratio between acetic acid and 1 is increased from 0.8 to 1.4, yields improve from 20 to 33% and remain almost constant at ratios up to 2. The reaction can be rationalized as shown in scheme 1.



1 2a

Scheme 1

Similarly, dimethylmalonate (150 mmoles) reacts with 1 (10 mmoles) at room temperature (3 days) giving the adduct 2b in about 20% yield. Compound 2b is rapidly hydrolysed during work up. Its isolation can be accomplished by extracting the reaction mixture, dissolved in ether, with 5% aqueous HCl. The aqueous layer is then very rapidly extracted with ether, immediately made alkaline with Na_2CO_3 and extracted five times with ether. Further purification can be achieved by GLC (10% OV-17, silicon oil on chromosorb, temp. 90°).

Compound 2b: Analysis calc. for $C_{10}H_{17}O_4N$: C 55.80; H 7.96; N 6.51, Found C 55.91; H 7.84; N 6.46

IR (liq. film): 3205, 3120 cm^{-1}, cyclopropyl C-H; 2960, 2820, 2770 cm^{-1}, C-H; 1735 cm^{-1}, C=O; 1020 cm^{-1}, cyclopropyl

NMR ($CDCl_3$): δ = 0.75 ppm, s (4H); δ = 2.28 ppm, s (6H); δ = 3.70 ppm, s (6H) and δ = 3.88 ppm, s (1H)

MS: $M^{\oplus}$ at m/e 215, 24% of the base peak at m/e 156.

Furthermore, treatment of 1 (50 mmoles) with phenol (100 mmoles) in CH_2Cl_2 at room temperature for 48 hrs, leads to the introduction of the 1-dimethylaminocyclopropyl group in the ortho position only, giving the cyclopropylphenol 2c in 54% yield.

1-(o-Hydroxyphenyl)1-dimethylaminocyclopropane 2c: Analysis calc. for $C_{11}H_{15}ON$: C 74.54; H 8.53; N 7.90, Found C 74.50; H 8.71; N 7.81

IR (KBr): 3400-2400 cm^{-1}, broad band (OH intramolecularly bonded); 3000-2800 cm^{-1}, $N(CH_3)_2$; 1600, 1520 cm^{-1}, Ar; 1020 cm^{-1}, cyclopropyl; 675 cm^{-1}, Ar (4 adjacent H-atoms)

NMR ($CDCl_3$): δ = 1.0 ppm, AA'BB' pattern (4H); δ = 2.3 ppm, s (6H); δ = 6.9 ppm, m (4H)

MS: $M^{\oplus}$ at m/e 177 (base peak).

Compound 2c reacts with phenylisocyanate giving the corresponding urethane; m.p. 51-52°. Analysis calc. for $C_{18}H_{20}O_2N_2$: C 72.95; H 6.80; N 9.45, Found C 72.64; H 6.91; N 9.49

IR (KBr): 3450 cm^{-1}, NH; 3100, 3000 cm^{-1}, cyclopropyl C-H, Ar-H; 1740 cm^{-1}, C=O; 1600, 1500 cm^{-1}, Ar; 1010 cm^{-1}, cyclopropyl

NMR (CD_3COCD_3): δ = 0.85 ppm, AA'BB' pattern (4H); δ = 2.2 ppm, s (6H); δ = 7.3 ppm, m (9H)

MS: $M^{\oplus}$ at m/e 296, 6% of the base peak at m/e 100.

Remarkably, such well known Mannich reagents[3,4] as succinimide, dinitroethane, methyl cyanoacetate, methyl acetoacetate and acetylacetone all fail to react in this way. Possibly this is due to amino-elimination[4] from the products or the reversal of the Mannich reaction[5]. This problem is currently being investigated.

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